


Applicant: Palsson, Bernhard	Docket No. 066662-0092	Serial No. 09/923,870
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Title: METHODS FOR IDENTIFYING DRUG TARGETS BASED ON GENOMIC SEQUENCE DATA	Patent No. _____
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 Form PTO 1449
 314 References attached
☐ Preliminary Amendment
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Applicant: Palsson, Bernhard	Docket No. 066662-0092	Serial No. 09/923,870
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Exhibit 1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : Customer Number: 41552
: :
Palsson, Bernhard : Confirmation Number: 1729
: :
Application No.: 09/923,870 : Group Art Unit: 1631
: :
Filed: August 06, 2001 : Examiner: NEGIN, Russell Scott
: :
For: METHODS FOR IDENTIFYING DRUG TARGETS BASED ON GENOMIC SEQUENCE
DATA

TRANSMITTAL

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING (37 CFR § 1.8(a))

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Carrie Hines

Sir:


Transmitted are the following:

1. Communication with Exhibit A attached
2. Three Hundred Fourteen (314) References

The Commissioner is hereby authorized to charge payment of any fees associated with this communication or credit any overpayment, to Deposit Account No. 502624, including any filing fees under 37 CFR 1.16 for presentation of extra claims and any patent application processing fees under 37 CFR 1.17.

Respectfully submitted,

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Date: July 9, 2009

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

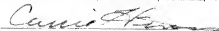
In re Application of : Customer Number: 41552
: Palsson, Bernhard : Confirmation Number: 1729
: Application No.: 09/923,870 : Group Art Unit: 1631
: Filed: August 06, 2001 : Examiner: NEGIN, Russell Scott
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DATA

COMMUNICATION

Mail Stop Amendment
Commissioner for Patents
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Alexandria, VA 22313-1450

CERTIFICATE OF MAILING (37 CFR, § 1.8(a))

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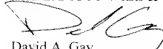
Sir:

Further to the Information Disclosure Statement and PTO Form 1449 filed June 18, 2009, provided herewith are copies of references cited in the Form 1449, but not provided with the previously filed Information Disclosure Statement. For the Examiner's convenience, the references are listed on the attached Exhibit A, and are identified by the original citation number included on the previously filed PTO Form 1449.

The Commissioner is hereby authorized to charge payment of any fees associated with this communication or credit any overpayment, to Deposit Account No. 502624, including any filing fees under 37 CFR 1.16 for presentation of extra claims and any patent application processing fees under 37 CFR 1.17.

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EXHIBIT A
U.S. Application No. 09/923,870

29.	Adamowicz, et al., "Nutritional complementation of oxidative glucose metabolism in <i>Escherichia coli</i> via pyrroloquinoline quinone-dependent glucose dehydrogenase and the Enter-Doudoroff pathway," <i>Appl Environ Microbiol</i> , 57(7):2012-2015 (1991).
30.	Alberty, "Calculation of Biochemical Net Reactions and Pathways by Using Matrix Operations," <i>Biophys J</i> , 71(1):507-515 (1996).
31.	Alm, et al., "Genomic-sequence comparison of two unrelated isolates of the human gastric pathogen <i>Helicobacter pylori</i> ," <i>Nature</i> , 397(6715):176-80 (1999).
32.	Alon, et al., "Broad patterns of gene expression revealed by clustering analysis of tumor and normal colon tissues probed by oligonucleotide arrays," <i>Proc Natl Acad Sci U.S.A.</i> , 96(12):6745-6750 (1999).
33.	Alter, et al., "Singular value decomposition for genome-wide expression data processing and modeling," <i>Proc Natl Acad Sci U.S.A.</i> , 97(18):10101-10106 (2000).
34.	Altschul, et al., "Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs," <i>Nucl Acids Res</i> , 25(17):3389-3402 (1997).
35.	Alves, et al., "Systemic properties of ensembles of metabolic networks: application of graphical and statistical methods to simple unbranched pathways," <i>Bioinformatics</i> , 16(6):534-547 (2000).
36.	Andre, "An overview of membrane transport proteins in <i>Saccharomyces cerevisiae</i> ," <i>Yeast</i> , 11(16):1575-1611 (1995).
37.	Anonymous, "The yeast genome directory" <i>Nature</i> , 387(6632 Suppl):5 (1997).
38.	Appel, et al., "A new generation of information retrieval tools for biologists: the example of the ExPASy WWW server," <i>Trends Biochem Sci</i> , 19(6):258-260 (1994).
39.	Attanoos, et al., "Ileostomy polyps, adenomas, and adenocarcinomas," <i>Gut</i> , 37(6):840-844 (1995).
40.	Baba, et al., "Construction of <i>Escherichia coli</i> K-12 in-frame, single-gene knockout mutants: the Keio collection," <i>Mol Syst Biol</i> , 2:2006-2008 (2006).
41.	Bailey, "Complex Biology With No Parameters," <i>Nat Biotechnol</i> , 19(6):503-504 (2001).
42.	Bailey, TL and Elkan, C, "Fitting a mixture model by expectation maximization to discover motifs in biopolymers," <i>Proc Int Conf Intell Syst Mol Biol</i> , 2:28-36 (1994).
43.	Bailey, TL and Gribskov, M, "Combining evidence using p-values: application to sequence homology searches," <i>Bioinformatics</i> , 14(1):48-54 (1998).
44.	Bairoch, A, and Apweiler, R, "The SWISS-PROT Protein Sequence database and its supplement TrEMBL in 2000," <i>Nucleic Acids Res</i> , 28(1):45-48 (2000).
45.	Ball, et al., "Integrating functional genomic information into the <i>Saccharomyces</i> genome database," <i>Nucleic Acids Res</i> , 28(1):77-80 (2000).
46.	Ban, et al., "Thymine and uracil catabolism in <i>Escherichia coli</i> ," <i>J Gen Microbiol</i> , 73(2):267-272 (1972).
47.	Bansal, "Integrating co-regulated gene-groups and pair-wise genome comparisons to automate reconstruction of microbial pathways," <i>Bioinformatics and Bioengineering Conference</i> , 209-216 (2001).
48.	Bard, et al., "Sterol mutants of <i>Saccharomyces cerevisiae</i> : chromatographic analyses," <i>Lipids</i> , 12(8):645-654 (1977).
49.	Baxevas, "The Molecular Biology Database Collection: 2002 update," <i>Nucleic Acids Res</i> , 30:1-12 (2002).
50.	Beard, et al., "Energy Balance for Analysis of Complex Metabolic Networks," <i>Biophys J</i> , 83(1):79-86 (2002).

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U.S. Application No. 09/923,870

51.	Beckers, et al., "Large-Scale Mutational Analysis for the Annotation of the Mouse Genome," <i>Curr Opin Chem Biol</i> , 6(1):17-23 (2002).
52.	Bell, et al., "Composition and functional analysis of the <i>Saccharomyces cerevisiae</i> trehalose synthase complex," <i>J Biol Chem.</i> , 273(50):33311-33319 (1998).
53.	Benson, et al., "GenBank," <i>Nucleic Acids Res</i> , 28(1):15-18 (2000).
54.	Berry, "Improving production of aromatic compounds in <i>Escherichia coli</i> by metabolic engineering," <i>Trends Biotechnol</i> , 14(7):250-256 (1996).
55.	Bialy, "Living on the Edges," <i>Nat Biotechnol</i> , 19(2):111-112 (2001).
56.	Bianchi, P, and Zanella, A, "Hematologically Important Mutations: Red Cell Pyruvate Kinase (Third Update)," <i>Blood Cells, Molecules, and Diseases</i> , 15:47-53 (2000).
57.	Biaudet, et al., "Micado - a network-oriented database for microbial genomes," <i>Comput Appl Biosci</i> , 13(4):431-438 (1997).
58.	Birkholz, "Fumarate reductase of <i>Helicobacter pylori</i> --an immunogenic protein," <i>J Med Microbiol</i> , 41(1):56-62 (1994).
59.	Birner, et al., "Roles of phosphatidylethanolamine and of its several biosynthetic pathways in <i>Saccharomyces cerevisiae</i> ," <i>Mol Biol Cell</i> , 12(4):997-1007 (2001).
60.	Blackstock, WP and Weir, MP, "Proteomics: quantitative and physical mapping of cellular proteins," <i>Trends Biotechnol</i> , 17(3):121-127 (1999).
61.	BMES/EMBS Conference, Proceedings of the First Joint, Vol. 2, p. 1217 (1999).
62.	Bochner, "New technologies to assess genotype-phenotype relationships," <i>Nat Rev Genet</i> , 4(4):309-314 (2003).
63.	Boles, E, et al., "Identification and characterization of MAE 1, the <i>Saccharomyces cerevisiae</i> structural gene encoding mitochondrial malic enzyme," <i>J Bacteriol.</i> , 180(11):2875-2882 (1998).
64.	Boles, et al., "A family of hexosephosphate mutases in <i>Saccharomyces cerevisiae</i> ," <i>Eur J Biochem</i> , 220(1):83-96 (1994).
65.	Boles, et al., "Characterization of a glucose-repressed pyruvate kinase (Pyk2p) in <i>Saccharomyces cerevisiae</i> that is catalytically insensitive to fructose-1,6-bisphosphate," <i>J Bacteriol</i> , 179(9):2987-2993 (1997).
66.	Bonarius, et al., "Metabolic flux analysis of hybridoma cells in different culture media using mass balances," <i>Biotechnol Bioeng</i> , 50(3):299-318 (1996).
67.	Bono, et al., "Reconstruction of amino acid biosynthesis pathways from the complete genome sequence," <i>Genome Research</i> , 8(3):203-210 (1998).
68.	Bottomley, et al., "Cloning, sequencing, expression, purification and preliminary characterization of a type II dehydroquinase from <i>Helicobacter pylori</i> ," <i>Biochem. J.</i> , 319(Pt 2):559-565 (1996).
69.	Bourot, S and Karst, F, "Isolation and characterization of the <i>Saccharomyces cerevisiae</i> SUT1 gene involved in sterol uptake," <i>Gene</i> , 165(1):97-102 (1995).
70.	Burgard, AP and Maranas, CD, "Probing the Performance Limits of the <i>Escherichia coli</i> Metabolic Network Subject to Gene Additions or Deletions," <i>Biotechnol Bioeng</i> , 74(5):364-375 (2001).
71.	Burgard, AP and Maranas, CD, "Review of the Enzymes and Metabolic Pathways (EMP) Database," <i>Metab Eng</i> , 3(3):193-194(2) (2001).
72.	Burgard, et al., "Minimal reaction sets for <i>Escherichia coli</i> metabolism under different growth requirements and uptake environments," <i>Biotechnol Prog</i> , 17(5):791-797 (2001).

EXHIBIT A
U.S. Application No. 09/923,870

73.	Burgard, et al., "Optknoack: a bilevel programming framework for identifying gene knockout strategies for microbial strain optimization," <i>Biotechnol Bioeng</i> , 84(6):647-657 (2003).
74.	Burns, "Acetyl-CoA carboxylase activity in <i>Helicobacter pylori</i> and the requirement of increased CO ₂ for growth," <i>Microbiology</i> , 141(Pt 12):3113-3118 (1995).
75.	
76.	
77.	Chalker, et al., "Systematic identification of selective essential genes in <i>Helicobacter pylori</i> by genome prioritization and allelic replacement mutagenesis," <i>J Bacteriol</i> , 183(4):1259-1268 (2001).
78.	Chen, et al., "Characterization of the respiratory chain of <i>Helicobacter pylori</i> ," <i>FEMS Immunol Med Microbiol</i> , 24(2):169-174 (1999).
79.	Cherry, et al., "SGD: <i>Saccharomyces</i> Genome Database," <i>Nucleic Acids Res</i> , 26(1):73-79 (1998).
80.	
81.	Ciriacy, M and Breitenbach, I, "Physiological effects of seven different blocks in glycolysis in <i>Saccharomyces cerevisiae</i> ," <i>J Bacteriol</i> , 139(1):152-160 (1979).
82.	Clarke, "Complete set of steady states for the general stoichiometric dynamical system," <i>J Chem Phys</i> , 75(10):4970-4979 (1981).
83.	Clarke, "Stoichiometric network analysis," <i>Cell Biophys</i> , 12:237-253 (1988).
84.	
85.	Clifton, D and Fraenkel, DG, "Mutant studies of yeast phosphofructokinase," <i>Biochemistry</i> , 21(8):1935-1942 (1982).
86.	Clifton, et al., "Glycolysis mutants in <i>Saccharomyces cerevisiae</i> ," <i>Genetics</i> , 88(1):1-11 (1978).
87.	Compan, I and Touati, D, et al., "Anaerobic activation of <i>arcA</i> transcription in <i>Escherichia coli</i> : roles of Fnr and ArcA," <i>Mol Microbiol</i> , 11(5):955-964 (1994).
88.	Costanzo, et al., "YPD, PombePD and WormPD: model organism volumes of the BioKnowledge library, an integrated resource for protein information," <i>Nucleic Acids Res</i> , 29(1):75-9 (2001).
89.	Cotter, et al., "Aerobic regulation of cytochrome d oxidase (<i>cydAB</i>) operon expression in <i>Escherichia coli</i> : roles of Fnr and ArcA in repression and activation," <i>Mol Microbiol</i> , 25(3):605-615 (1997).
90.	
91.	Covert, et al., "Metabolic Modeling of Microbial Strains <i>In Silico</i> ," <i>Trends Biochem Sci</i> , 26(3):179-186 (2001).
92.	Covert, et al., "Regulation of Gene Expression in Flux Balance Models of Metabolism," <i>J Theor Biol</i> , 213(1):73-88 (2001).
93.	Covert, MW and Palsson, BO, "Constraints-based models: Regulation of Gene Expression Reduces the Steady-state Solution Space," <i>J Theor Biol</i> , 216 (2003).
94.	Covert, MW and Palsson, BO, "Transcriptional Regulation in Constraints-based Metabolic Models of <i>Escherichia coli</i> ," <i>J Biol Chem</i> , 277(31):28058- 28064 (2002).
95.	Cupp, JR and McAlister-Henn, L., "Cloning and Characterization of the gene encoding the IDH1 subunit of NAD(+)-dependent isocitrate dehydrogenase from <i>Saccharomyces cerevisiae</i> ," <i>J Biol Chem</i> , 267(23):16417-16423 (1992).
96.	D'Haeseleer, et al., "Genetic network inference: from co-expression clustering to reverse engineering," <i>Bioinformatics</i> , 16(8):707-726 (2000).

EXHIBIT A
U.S. Application No. 09/923,870

97.	Danchin, "Comparison Between the Escherichia coli and Bacillus subtilis Genomes Suggests That a Major Function of Polynucleotide Phosphorylase is to Synthesize CDP," <i>DNA Research</i> , 4(1):9-18 (1997).
98.	Dandekar, et al., "Pathway Alignment: Application to the Comparative Analysis of Glycolytic Enzymes," <i>Biochem J</i> , 343(Pt 1):115-124 (1999).
99.	Dantigny, et al., "A new control strategy for yeast production based on the L/A* approach," <i>Appl Microbiol Biotechnol</i> , 36:352-357 (1991).
100.	Datsenko, KA and Wanner, BL, "One-step inactivation of chromosomal genes in <i>Escherichia coli</i> K-12 using PCR products," <i>Proc Natl Acad Sci U.S.A.</i> , 97(12):6640-6645 (2000).
101.	Daum, et al., "Biochemistry, cell biology and molecular biology of lipids of <i>Saccharomyces cerevisiae</i> ," <i>Yeast</i> , 14(16):1471-1510 (1998).
102.	Daum, et al., "Systematic analysis of yeast strains with possible defects in lipid metabolism," <i>Yeast</i> , 15(7):601-614 (1999).
103.	Dauner, et al., " <i>Bacillus subtilis</i> Metabolism and Energetics in Carbon-Limited and Excess-Carbon Chemostat Culture," <i>J Bacteriol</i> , 183(24):7308-7317 (2001).
104.	Dauner, et al., "Metabolic Flux Analysis with a Comprehensive Isotopomer Model in <i>Bacillus subtilis</i> ," <i>Biotechnol Bioeng</i> , 76(2):144-156 (2001).
105.	Dauner, M and Sauer, U, "Stoichiometric Growth Model for Riboflavin-Producing <i>Bacillus subtilis</i> ," <i>Biotechnol Bioeng</i> , 76(1):132-143 (2001).
106.	de Jong, H., "Modeling and simulation of genetic regulatory systems: a literature review," <i>J Comput Biol</i> , 9(1):67-103 (2002).
107.	De Reuse, et al., "The <i>Helicobacter pylori</i> ureC gene codes for a phosphoglucosamine mutase," <i>J Bacteriol</i> , 179(11):3488-3493 (1997).
108.	Delgado and Liao, "Identifying Rate-Controlling Enzymes in Metabolic Pathways without Kinetic Parameters," <i>Biotechnol Prog</i> , 7:15-20 (1991).
109.	Demain, et al., "Cellulase, clostridia, and ethanol," <i>Microbiol Mol Biol Rev</i> , 69(1):124-154 (2005).
110.	Department of Energy, <i>Breaking the Biological Barriers to Cellulosic Ethanol</i> (2006).
111.	DeRisi, et al., "Exploring the Metabolic and Genetic Control of Gene Expression on a Genomic Scale," <i>Science</i> , 278(5338):680-686 (1997).
112.	Devine, KM, "The <i>Bacillus subtilis</i> Genome Project: Aims and Progress," <i>Trends Biotechnol</i> , 13(6):210-216 (1995).
113.	Dickson, "Sphingolipid Functions in <i>Saccharomyces Cerevisiae</i> : Comparison to Mammals," <i>Annu Rev Biochem</i> , 67:27-48 (1998).
114.	Dickson, et al., "Serine palmitoyltransferase," <i>Methods Enzymol</i> , 311:3-9 (2000).
115.	DiRusso, CC and Black, PN, "Long-chain fatty acid transport in bacteria and yeast. Paradigms for defining the mechanism underlying this protein-mediated process," <i>Mol Cell Biochem</i> , 192(1-2):41-52 (1999).
116.	
117.	Edwards, et al., "Characterizing the Metabolic Phenotype: A Phenotype Phase Plane Analysis," <i>Biotech Bioeng</i> , 77(1):27-36 (2002).
118.	Edwards, et al., "In Silico Predictions of <i>Escherichia coli</i> metabolic capabilities are Consistent with Experimental Data," <i>Nat Biotechnol</i> , 19(2):125-130 (2001).
119.	Edwards, JS and Palsson, BO, "Robustness analysis of the <i>Escherichia coli</i> metabolic network," <i>Biotechnol Prog</i> , 16(6):927-939 (2000).

EXHIBIT A
U.S. Application No. 09/923,870

120.	Edwards, JS, and Palsson, BO. "Metabolic flux balance analysis and the <i>in silico</i> analysis of Escherichia coli K-12 gene deletions," <i>BMC Bioinformatics</i> , 1:1-10 (2000).
121.	Eisen, et al., "Cluster analysis and display of genome-wide expression patterns," <i>Proc Natl Acad Sci U.S.A.</i> , 95:14863-14868 (1998).
122.	Eisenberg, et al., "Protein Function in the Post-Genomic Era," <i>Nature</i> , 405(6788):823-826 (2000).
123.	Ermolaeva, et al., "Prediction of Operons in Microbial Genomes," <i>Nucl Acids Research</i> , 29(5):1216-1221 (2001).
124.	
125.	Fiehn, "Metabolomics--the link between genotypes and phenotypes," <i>Plant Mol Biol</i> , 48(1-2):155-171 (2002).
126.	Finel, "Does NADH play a central role in energy metabolism in Helicobacter pylori?," <i>Trends Biochem Sci</i> , 23(11):412-413 (1998).
127.	Fiorelli, et al., "Chronic non-spherocytic haemolytic disorders associated with glucose-6-phosphate dehydrogenase variants," <i>Bailliere's Clinical Haematology</i> , 13:39-55 (2000).
128.	
129.	Flikweert, et al., "Pyruvate decarboxylase: an indispensable enzyme for growth of <i>Saccharomyces cerevisiae</i> on glucose.," <i>Yeast</i> , 12(3):247-257 (1996).
130.	Forst, "Network genomics-- A Novel approach for the analysis of biological systems in the post-genomic era," <i>Molecular Biology Reports</i> , 29(3):265-280 (2002).
131.	Forster, et al., "Large-scale evaluation of <i>in silico</i> gene deletions in <i>Saccharomyces cerevisiae</i> ," <i>Omic</i> , 7(2):193-202 (2003).
132.	Fraenkel, "The accumulation of glucose 6-phosphate from glucose and its effect in an Escherichia coli mutant lacking phosphoglucose isomerase and glucose 6-phosphate dehydrogenase," <i>J Biol Chem</i> , 243(24):6451-6457 (1968).
133.	Fraser, et al., "Microbial genome sequencing," <i>Nature</i> , 406:799-803 (2000).
134.	Fromont-Racine, et al., "Toward a functional analysis of the yeast genome through exhaustive two-hybrid screens," <i>Nat Genet</i> , 16(3):277-282 (1997).
135.	Fukuchi, et al., "Isolation, overexpression and disruption of a <i>Saccharomyces cerevisiae</i> YNK gene encoding nucleoside diphosphate kinase," <i>Genes</i> , 129(1):141-146 (1993).
136.	Gaasterland, T. and Selkov, E., "Reconstruction of Metabolic Networks Using Incomplete Information," <i>Proc Int Conf Intell Syst Mol Biol</i> , 3:127-135 (1995).
137.	Gancedo, C and Delgado, MA, "Isolation and characterization of a mutant from <i>Saccharomyces cerevisiae</i> lacking fructose 1,6-bisphosphatase," <i>Eur J Biochem</i> , 139:651-655 (1984).
138.	Gangloff, et al., "Molecular cloning of the yeast mitochondrial aconitase gene (ACO1) and evidence of a synergistic regulation of expression by glucose plus glutamate," <i>Mol Cell Biol</i> , 10(7):3551-3561 (1990).
139.	
140.	Glasner, et al., "ASAP, a systematic annotation package for community analysis of genomes," <i>Nucleic Acids Res</i> , 31(1):147-151 (2003).
141.	Goffeau, A, "Four years of post-genomic life with 6000 yeast genes," <i>FEBS Lett</i> , 480(1):37-41 (2000).
142.	Goryanin, et al., "Mathematical simulation and analysis of cellular metabolism and regulation," <i>Bioinformatics</i> , 15(9):749-758 (1999).

EXHIBIT A
U.S. Application No. 09/923,870

143	Goto, et al., "LIGAND database for enzymes, compounds and reactions," <u>Nucleic Acids Res</u> , 27(1):377-379 (1999).
144	Goto, et al., "LIGAND: chemical database for enzyme reactions," <u>Bioinformatics</u> , 14(7):591-599 (1998).
145	Grewal, et al., "Computer Modelling of the Interaction Between Human Choriogonadotropin and Its Receptor," <u>Protein Engineering</u> , 7(2):205-211 (1994).
146	Griffin, et al., "Complementary profiling of gene expression at the transcriptome and proteome levels in <i>Saccharomyces cerevisiae</i> ," <u>Mol Cell Proteomics</u> , 1:323-333 (2002).
147	Grundy, et al., "Regulation of the <i>Bacillus subtilis</i> acetate kinase gene by CcpA," <u>J Bacteriol</u> , 175(22):7348-7355 (1993).
148	Guelzim, et al., "Topological and causal structure of the yeast transcriptional regulatory network," <u>Nat Genet</u> , 31(1):60-63 (2002).
149	Guetsova, et al., "The isolation and characterization of <i>Saccharomyces cerevisiae</i> mutants that constitutively express purine biosynthetic genes," <u>Genetics</u> , 147(2):383-397 (1997).
150	
151	Hardison, et al., "Globin Gene Server: A Prototype E-Mail Database Server Featuring Extensive Multiple Alignments and Data Compilation for Electronic Genetic Analysis," <u>Genomics</u> , 21(2):344-353 (1994).
152	Hartig, et al., "Differentially regulated malate synthase genes participate in carbon and nitrogen metabolism of <i>S. cerevisiae</i> ," <u>Nucleic Acids Res</u> , 20(21):5677-5686 (1992).
153	Hasty, et al., "Computational Studies of Gene Regulatory Networks: <i>In Numero Molecular Biology</i> ," <u>Nat Rev Genet</u> , 2(4):268-279 (2001).
154	Hata, et al., "Characterization of a <i>Saccharomyces cerevisiae</i> mutant, N22, defective in ergosterol synthesis and preparation of [28-14C]ergosta-5,7-dien-3 beta-ol with the mutant," <u>J Biochem</u> , 94(2):501-510 (1983).
155	Hatzimanikatis, et al., "Analysis and Design of Metabolic Reaction Networks Via Mixed-Integer linear Optimization," <u>AIChE Journal</u> , 42(5):1277-1292 (1996).
156	Hazell, et al., "How <i>Helicobacter pylori</i> works: an overview of the metabolism of <i>Helicobacter pylori</i> ," <u>Helicobacter</u> , 2(1):1-12 (1997).
157	Heijnen, et al., "Application of balancing methods in modeling the penicillin fermentation," <u>Biotechnology & Bioeng.</u> , 21:2175-2201 (1979).
158	Heinisch, et al., "Investigation of two yeast genes encoding putative isoenzymes of phosphoglycerate mutase," <u>Yeast</u> , 14(3):203-213 (1998).
159	Heinrich, et al., "Metabolic regulation and mathematical models," <u>Prog Biophys Mol Biol</u> , 32(1):1-82 (1977).
160	Heinrich, et al., "Stoichiometric Analysis," <u>The Regulation of Cellular Systems</u> , xix:75-111 and 372, Chapman & Hall, New York (1996).
161	Henriksen, et al., "Growth energetics and metabolism fluxes in continuous cultures of <i>Penicillium chrysogenum</i> ," <u>J of Biotechnol</u> , 45(2):149-164 (1996).
162	Heyer, et al., "Exploring expression data: identification and analysis of coexpressed genes," <u>Genome Res</u> , 9(11):1106-1115 (1999).
163	Holter, et al., "Dynamic modeling of gene expression data," <u>Proc Natl Acad Sci U.S.A.</u> , 98(4):1693-1698 (2001).
164	Holter, et al., "Fundamental patterns underlying gene expression profiles: simplicity from complexity," <u>Proc Natl Acad Sci U.S.A.</u> , 97:8409-8414 (2000).
165	Houghten, "Generation and use of synthetic peptide combinatorial libraries for basic research and drug discovery," <u>Nature</u> , 354(6348):84-86 (1991).

EXHIBIT A
U.S. Application No. 09/923,870

166	Hughes, et al., "Functional discovery via a compendium of expression profiles," <i>Cell</i> , 102(1):109-126 (2000).
167	Hughes, et al., "Helicobacter pylori porCDAB and oodABC genes encode distinct pyruvate: flavodoxin and 2-oxoglutarate:acceptor oxidoreductases which mediate electron transport to NADP," <i>J Bacteriol</i> , 180(5):1119-1128 (1998).
168	Ideker, et al., "Integrated Genomic and Proteomic Analyses of a Systematically Perturbed Metabolic Network," <i>Science</i> , 292(5518):929-934 (2001).
169	Ince, JE and Knowles, CJ, "Ethylene formation by cell-free extracts of <i>Escherichia coli</i> ," <i>Arch Microbiol</i> , 146(2):151-158 (1986).
170	Ishii, et al., "DBTBS: a database of <i>Bacillus subtilis</i> promoters and transcription factors," <i>Nucleic Acids Res</i> , 29(1):278-280 (2001).
171	Iyer, et al., "Genomic binding sites of the yeast cell-cycle transcription factors SBF and MBF," <i>Nature</i> , 409(6819):533-538 (2001).
172	Jamshidi, et al., "Dynamic simulation of the human red blood cell metabolic network," <i>Bioinformatics</i> , 17(3):286-287 (2001).
173	Jamshidi, et al., "In silico model-driven assessment of the effects of single nucleotide polymorphisms (SNPs) on human red blood cell-metabolism," <i>Genome Research</i> , 12(11):1687-1692 (2002).
174	Jenkins, LS and Nunn, WD, "Genetic and molecular characterization of the genes involved in short-chain fatty acid degradation in <i>Escherichia coli</i> : the ato system," <i>J Bacteriol</i> , 169(1):42-52 (1987).
175	Jensen, et al., "A Literature Network of Human Genes for High-Throughput Analysis of Gene Expression," <i>Nat Genet</i> , 28(1):21-28 (2001).
176	Jorgensen, et al., "Metabolic flux distributions in <i>Penicillium chrysogenum</i> during fed-batch cultivations," <i>Biotechnol Bioeng</i> , 46(2):117-131 (1995).
177	Joshi, A and Palsson, BO, "Metabolic dynamics in the human red cell. Part I--A comprehensive kinetic model," <i>J Theor Biol</i> , 141(4):515-528 (1989).
178	Juty, et al., "Simultaneous Modeling of Metabolic, Genetic, and Product-Interaction Networks," <i>Briefings in Bioinformatics</i> , 2(3):223-232 (2001).
179	Kanehisa, M and Goto, S, "Kyoto Encyclopedia of Genes and Genomes database (KEGG)," <i>Nucleic Acids Res</i> , 28(1):27-30 (2000).
180	Karp, "An ontology for biological function based on molecular interactions," <i>Bioinformatics</i> , 16(3):269-285 (2000).
181	Karp, et al., "EcoCyc: encyclopedia of <i>Escherichia coli</i> genes and metabolism," <i>Nucleic Acids Res</i> , 27(1):55-58 (1999).
182	Karp, et al., "HinCyc: A knowledge base of the complete genome and metabolic pathways of <i>H. influenzae</i> ," <i>Proc Int Conf Intell Syst Mol Biol</i> , 4:116-124 (1996).
183	Karp, et al., "Integrated pathway-genome databases and their role in drug discovery," <i>Trends Biotechnol</i> , 17(7):275-281 (1999).
184	Karp, et al., "The EcoCyc and MetaCyc databases," <i>Nucleic Acids Research</i> , 28(1):56-59 (2000).
185	Kather, et al., "Another unusual type of citric acid cycle enzyme in <i>Helicobacter pylori</i> : the malate:quinone oxidoreductase," <i>J Bacteriol</i> , 182(11):3204-3209 (2000).
186	Keating, et al., "An ethanologenic yeast exhibiting unusual metabolism in the fermentation of lignocellulosic hexose sugars," <i>J Ind Microbiol Biotechnol</i> , 31(5):235-244 (2004).
187	

EXHIBIT A
U.S. Application No. 09/923,870

188	Kim, et al., "Saccharomyces cerevisiae contains two functional citrate synthase genes," <i>Mol Cell Biol</i> , 6(6):1936-1942 (1986).
189	Kirkman, et al., "Red cell NADP+ and NADPH in glucose-6-phosphate dehydrogenase deficiency," <i>Journal of Clinical Investigation</i> , 55(4):875-878 (1975).
190	Kremling, et al., "The organization of metabolic reaction networks. III. Application for diauxic growth on glucose and lactose," <i>Metab Eng</i> , 3(4):362-379 (2001).
191	Kunst, et al., "The Complete Genome Sequence of the Gram-positive Bacterium <i>Bacillus subtilis</i> ," <i>Nature</i> , 390(6557):249-256 (1997).
192	Lacroute, "Regulation of pyrimidine biosynthesis in <i>Saccharomyces cerevisiae</i> " <i>J Bacteriol</i> , 95(3):824-832 (1968).
193	Latif, F and Rajoka, MI, "Production of ethanol and xylitol from corn cobs by yeasts," <i>Bioresour Technol</i> , 77(1):57-63 (2001).
194	Lendenmann, U and Egli, T, "Is <i>Escherichia coli</i> growing in glucose-limited chemostat culture able to utilize other sugars without lag?," <i>Microbiology</i> , 141(Pt 1):71-78 (1995).
195	Leyva-Vasquez, MA and Setlow, P, "Cloning and nucleotide sequences of the genes encoding triose phosphate isomerase, phosphoglycerate mutase, and enolase from <i>Bacillus subtilis</i> ," <i>J Bacteriol</i> , 176(13):3903-3910 (1994).
196	Li, C and Wong, WH, "Model-based analysis of oligonucleotide arrays: expression index computation and outlier detection," <i>Proc Natl Acad Sci U.S.A.</i> , 98(1):31-36 (2001).
197	Liao, et al., "Pathway Analysis, Engineering, and Physiological Considerations for Redirecting Central Metabolism," <i>Biotechnol Bioeng</i> , 52(1):129-140 (1996).
198	Liao, JC and Oh, MK, "Toward predicting metabolic fluxes in metabolically engineered strains," <i>Metab Eng</i> , 1(3):214-223 (1999).
199	Link, et al., "Methods for generating precise deletions and insertions in the genome of wild-type <i>Escherichia coli</i> . Application to open reading frame characterization," <i>J Bacteriol</i> , 179(20):6228-6237 (1997).
200	Lofus, et al., "Isolation, characterization, and disruption of the yeast gene encoding cytosolic NADP-specific isocitrate dehydrogenase," <i>Biochemistry</i> , 33(32):9661-9667 (1994).
201	Lopez, et al., "The yeast inositol monophosphatase is a lithium- and sodium-sensitive enzyme encoded by a non-essential gene pair," <i>Mol Microbiol</i> , 31(4):1255-1264 (1999).
202	
203	Maier, et al., "Hydrogen uptake hydrogenase in <i>Helicobacter pylori</i> ," <i>FEMS Microbiol Lett</i> , 141(1):71-76 (1996).
204	Marcelli, et al., "The respiratory chain of <i>Helicobacter pylori</i> : identification of cytochromes and the effects of oxygen on cytochrome and menaquinone levels," <i>FEMS Microbiol Lett</i> , 138(1):59-64 (1996).
205	
206	McAdams, III and Arkin, A, "Simulation of Prokaryotic Genetic Circuits," <i>Annual Review of Biophysics and Biomolecular Structure</i> , 27:199-224 (1998).
207	
208	McAlister-Henn, L and Thompson, LM, "Isolation and expression of the gene encoding yeast mitochondrial malate dehydrogenase," <i>J Bacteriol</i> , 169(11):5157-5166 (1987).
209	McGee, D.J., "Helicobacter pylori rocF is required for arginase activity and acid protection in vitro but is not essential for colonization of mice or for urease activity," <i>J Bacteriol</i> , 165(1):65-76 (1998).

EXHIBIT A
U.S. Application No. 09/923,870

210.	Meldrum, "Automation for genomics, part one: preparation for sequencing," <u>Genome Res.</u> 10(8):1081-1092 (2000).
211.	Mendes, P and Kell, D, "Non-linear optimization of biochemical pathways: Applications to metabolic engineering and parameter estimation," <u>Bioinformatics.</u> 14(10):869-883 (1998).
212.	Mendz, et al., "Characterisation of glucose transport in <i>Helicobacter pylori</i> ," <u>Biochim Biophys Acta</u> , 1244(2-3):269-276 (1995).
213.	Mendz, et al., "Characterization of fumarate transport in <i>Helicobacter pylori</i> ," <u>J Membr Biol</u> , 165(1):65-76 (1998).
214.	Mendz, et al., "De novo synthesis of pyrimidine nucleotides by <i>Helicobacter pylori</i> ," <u>J Appl Bacteriol</u> , 77(1):1-8 (1994).
215.	
216.	
217.	Mendz, et al., "In situ characterization of <i>Helicobacter pylori</i> arginase," <u>Biochim Biophys Acta</u> , 1388(2):465-477 (1998).
218.	Mendz, et al., "Purine metabolism and the microaerophily of <i>Helicobacter pylori</i> ," <u>Arch Microbiol</u> , 168(6):448-456 (1997).
219.	Mendz, et al., "The Entner-Doudoroff pathway in <i>Helicobacter pylori</i> ," <u>Arch Biochem Biophys</u> , 312(2):349-356 (1994).
220.	Mendz, GL and Hazell SL, "Aminoacid utilization by <i>Helicobacter pylori</i> ," <u>Int J Biochem Cell Biol</u> , 27(10):1085-1093 (1995).
221.	
222.	Mendz, GL and Hazell, SL, "Glucose phosphorylation in <i>Helicobacter pylori</i> ," <u>Arch Biochem Biophys</u> , 300(1):522-525 (1993).
223.	Mendz, GL, et al., "Pyruvate metabolism in <i>Helicobacter pylori</i> ," <u>Arch Microbiol</u> , 162(3):187-192 (1994).
224.	
225.	Mewes, et al., "MIPS: A database for genomes and protein sequences," <u>Nucleic Acids Research</u> , 30(1):31-34 (2002).
226.	Mitchell, "The GLN1 locus of <i>Saccharomyces cerevisiae</i> encodes glutamine synthetase," <u>Genetics</u> , 111(2):243-258 (1985).
227.	Moszer, "The Complete Genome of <i>Bacillus Subtilis</i> : From Sequence Annotation to Data Management and Analysis," <u>FEBS Lett</u> , 430(1-2):28-36 (1998).
228.	Moszer, et al., "SubtiList: the reference database for the <i>bacillus subtilis</i> genome," <u>Nucleic Acids Res</u> , 30(1):62-65 (2002).
229.	Mulquinney, PJ and Kuchel, PW, "Model of 2,3-bisphosphoglycerate metabolism in the human erythrocyte based on detailed enzyme kinetic equations: computer simulation and metabolic control analysis," <u>Biochem J</u> , 342(Pt 3):597-604 (1999).
230.	Murray, M and Greenberg, ML, "Expression of yeast INM1 encoding inositol monophosphatase is regulated by inositol, carbon source and growth stage and is decreased by lithium and valproate," <u>Mol Microbiol</u> , 36(3):651-661 (2000).
231.	Nedenskov, "Nutritional requirements for growth of <i>Helicobacter pylori</i> ," <u>Appl Environ Microbiol</u> , 60(9):3450-3453 (1994).
232.	Nissen, et al., "Expression of a cytoplasmic transhydrogenase in <i>Saccharomyces cerevisiae</i> results in formation of 2-oxoglutarate due to depletion of the NADPH pool," <u>Yeast</u> , 18(1):19-32 (2001).
233.	Nissen, et al., "Flux distributions in anaerobic, glucose-limited continuous cultures of <i>Saccharomyces cerevisiae</i> ," <u>Microbiology</u> , 143(Pt 1):203-218 (1997).

EXHIBIT A
U.S. Application No. 09/923,870

234.	Ogasawara, "Systematic function analysis of <i>Bacillus subtilis</i> genes," <i>Res Microbiol</i> , 151(2):129-134 (2000).
235.	Ogata, et al., "KEGG: Kyoto Encyclopedia of Genes and Genomes," <i>Nucleic Acids Res</i> , 27(1):29-34 (1999).
236.	Oh, MK and Liao, JC, "Gene expression profiling by DNA microarrays and metabolic fluxes in <i>Escherichia coli</i> ," <i>Biotech Prog</i> , 16:278-286 (2000).
237.	Olsson, et al., "Separate and simultaneous enzymatic hydrolysis and fermentation of wheat hemicellulose with recombinant xylose utilizing <i>Saccharomyces cerevisiae</i> ," <i>Appl Biochem Biotechnol</i> , 129-132:117-129 (2006).
238.	Otto, et al., "A mathematical model for the influence of fructose 6-phosphate, ATP, potassium, ammonium and magnesium on the phosphofructokinase from rat erythrocytes," <i>Eur J Biochem</i> , 49(1):169-178 (1974).
239.	Ouzounis, CA and Karp, PD, "Global Properties of the Metabolic Map of <i>Escherichia coli</i> ," <i>Genome Res</i> , 10(4):568-576 (2000).
240.	Overbeek, et al., "WIT: Integrated System for High-Throughput Genome Sequence Analysis and Metabolic Reconstruction" <i>Nucleic Acids Res</i> , 28(1):123-125 (2000).
241.	Overkamp, et al., "In vivo analysis of the mechanisms for oxidation of cytosolic NADH by <i>Saccharomyces cerevisiae</i> mitochondria," <i>J Bacteriol</i> , 182(10):2823-2830 (2000).
242.	Ozcan, S., Freidel, K., Leuker, A. & Ciriacy, M., "Glucose uptake and catabolite repression in dominant HTR1 mutants of <i>Saccharomyces cerevisiae</i> ," <i>J Bacteriol</i> , 175(17):5520-5528 (1993).
243.	Pallotta, et al., "Saccharomyces cerevisiae mitochondria can synthesise FMN and FAD from externally added riboflavin and export them to the extramitochondrial phase," <i>FEBS Lett</i> , 428(3):245-249 (1998).
244.	Palmieri, et al., "Identification and functions of new transporters in yeast mitochondria," <i>Biochim Biophys Acta</i> , 1459(2-3):363-369 (2000).
245.	Palmieri, et al., "Identification of the yeast ACR1 gene product as a succinate-fumarate transporter essential for growth on ethanol or acetate," <i>FEBS Lett</i> , 417(1):114-118 (1997).
246.	Palmieri, et al., "Identification of the yeast mitochondrial transporter for oxaloacetate and sulfate," <i>J Biol Chem</i> , 274(32):22184-22190 (1999).
247.	Palmieri, et al., "Yeast mitochondrial carriers: bacterial expression, biochemical identification and metabolic significance," <i>J Bioenerg Biomembr</i> , 32(1):67-77 (2000).
248.	Palsson, "The Challenges of in Silico Biology," <i>Nat Biotechnol</i> , 18(11):1147-1150 (2000).
249.	Papin, et al., "The genome-scale metabolic extreme pathway structure in <i>Haemophilus influenzae</i> shows significant network redundancy," <i>J Theor Biol</i> , 215(1):67-82 (2002).
250.	Parks, "Metabolism of sterols in yeast," <i>CRC Crit Rev Microbiol</i> , 6(4):301-341 (1978).
251.	Parks, et al., "Use of sterol mutants as probes for sterol functions in the yeast, <i>Saccharomyces cerevisiae</i> ," <i>Crit Rev Biochem Mol Biol</i> , 34(6):399-404 (1999).
252.	
253.	Paulsen, et al., "Unified inventory of established and putative transporters encoded within the complete genome of <i>Saccharomyces cerevisiae</i> ," <i>FEBS Lett</i> , 430(1-2):116-125 (1998).
254.	Pearson, et al., "Comparison of DNA Sequences With Protein Sequences," <i>Genomics</i> , 46(1):24-36 (1997).
255.	Persson, et al., "Phosphate permeases of <i>Saccharomyces cerevisiae</i> : structure, function and regulation," <i>Biochim Biophys Acta</i> , 1422(3):255-272 (1999).

EXHIBIT A
U.S. Application No. 09/923,870

256.	Peterson, et al., "The Comprehensive Microbial Resource," <u>Nucleic Acids Res.</u> 29(1):123-125 (2001).
257.	Pharkya, et al., "Exploring the overproduction of amino acids using the bilevel optimization framework OptKnock," <u>Biotechnol Bioeng.</u> 84(7):887-899 (2003).
258.	Phelps, et al., "Metabolomics and microarrays for improved understanding of phenotypic characteristics controlled by both genomics and environmental constraints," <u>Curr Opin Biotechnol.</u> 13(1):20-24 (2002).
259.	Pitson, et al., "The tricarboxylic acid cycle of <i>Helicobacter pylori</i> ," <u>Eur J Biochem.</u> 260(1):258-267 (1999).
260.	Price, et al., "Determination of redundancy and systems properties of the metabolic network of <i>Helicobacter pylori</i> using genome-scale extreme pathway analysis," <u>Genome Res.</u> 12(5):760-769 (2002).
261.	Price, et al., "Genome-scale models of microbial cells: evaluating the consequences of constraints," <u>Nat Rev Microbiol.</u> 2(11):886-897 (2004).
262.	Price, et al., "Network-based analysis of metabolic regulation in the human red blood cell," <u>J Theor Biol.</u> 225(2):185-194 (2003).
263.	Przybyla-Zawislak, et al., "Genes of succinyl-CoA ligase from <i>Saccharomyces cerevisiae</i> ," <u>Eur J Biochem.</u> 258(2):736-743 (1998).
264.	Qian, et al., "Ethanol production from dilute-Acid softwood hydrolysate by co-culture," <u>Appl Biochem Biotechnol.</u> 134(3):273-284 (2006).
265.	Reed, et al., "An expanded genome-scale model of <i>Escherichia coli</i> K-12 (iJR904 GSM/GPR)," <u>Genome Biol.</u> 4(9):R54 (2003).
266.	Reed, JL and Palsson, BO, "Thirteen years of building constraint-based in silico models of <i>Escherichia coli</i> " <u>J Bacteriol.</u> 185(9):2692-2699 (2003).
267.	Regenberg, et al., "Substrate specificity and gene expression of the amino-acid permeases in <i>Saccharomyces cerevisiae</i> ," <u>Curr Genet.</u> 36(6):317-328 (1999).
268.	Remize, et al., "Engineering of the pyruvate dehydrogenase bypass in <i>Saccharomyces cerevisiae</i> : role of the cytosolic Mg(2+) and mitochondrial K(+) acetaldehyde dehydrogenases Ald6p and Ald4p in acetate formation during alcoholic fermentation," <u>Appl Environ Microbiol.</u> 66(8):3151-3159 (2000).
269.	Ren, et al., "Genome-wide location and function of DNA binding proteins," <u>Science.</u> 290(5500):2306-2309 (2000).
270.	Repetto, B and Tzagoloff, A, "In vivo assembly of yeast mitochondrial alpha-ketoglutarate dehydrogenase complex," <u>Mol Cell Biol.</u> 11(8):3931-3939 (1991).
271.	Reynolds, DJ and Penn, CW, "Characteristics of <i>Helicobacter pylori</i> growth in a defined medium and determination of its amino acid requirements," <u>Microbiology.</u> 140(Pt 10):2649-2656 (1994).
272.	Rhee, et al., "Activation of gene expression by a ligand-induced conformational change of a protein-DNA complex," <u>J Biol Chem.</u> 273(18):11257-11266 (1998).
273.	Romero, PR and Karp, P, "Nutrient-Related Analysis of Pathway/Genome Databases," <u>Pac Symp Biocomput.</u> 471-482 (2001).
274.	Saier, MH, "Genome sequencing and informatics: new tools for biochemical discoveries," <u>Plant Physiol.</u> 117(4):1129-1133 (1998).
275.	Salgado, et al., <u>Nucleic Acids Res.</u> 29(1):72-74 (2001).
276.	Salmon, et al., "Global gene expression profiling in <i>Escherichia coli</i> K12. The effects of oxygen availability and FNR," <u>J Biol Chem.</u> 278(32):29837-29855 (2003).
277.	Sauer, et al., "Metabolic flux ratio analysis of genetic and environmental modulations of <i>Escherichia coli</i> central carbon metabolism," <u>J Bacteriol.</u> 181(21):6679-6688 (1999).

EXHIBIT A
U.S. Application No. 09/923,870

278.	Sauer, U and Bailey, JE, "Estimation of P-to-O Ratio in <i>Bacillus subtilis</i> and Its Influence on Maximum Riboflavin Yield," <u>Biotechnol Bioeng</u> , 64(6):750-754 (1999).
279.	Sauer, Uwe, "Evolutionary Engineering of Industrially Important Microbial Phenotypes," <u>Adv in Biochem Eng Biotechnol</u> , 73:129-169 (2001).
280.	Savageau, "Biochemical systems analysis. I. Some mathematical properties of the rate law for the component enzymatic reactions," <u>J Theor Biol</u> , 25(3):365-369 (1969).
281.	Schaaff-Gerstenschlager, I and Zimmermann, FK, "Pentose-phosphate pathway in <i>Saccharomyces cerevisiae</i> : analysis of deletion mutants for transketolase, transaldolase, and glucose 6-phosphate dehydrogenase," <u>Curr Genet</u> , 24(5):373-376 (1993).
282.	Schaff, et al., "the Virtual cell" <u>Proceedings of the Pacific Symposium on Biocomputing</u> , 4:228-239 (1999).
283.	
284.	Schilling, "On Systems Biology and the Pathway Analysis of Metabolic Networks," Department of Bioengineering, University of California, San Diego: La Jolla, p. 198-241 (2000).
285.	Schilling, CH and Palsson, BO, "Assessment of the Metabolic Capabilities of <i>Haemophilus influenzae</i> Rd Through a Genome-scale Pathway Analysis," <u>J Theor Biol</u> , 203(3):249-283 (2000).
286.	Schilling, CH and Palsson, BO, "The Underlying Pathway Structure of Biochemical Reaction Networks," <u>Proc Natl Acad Sci U.S.A.</u> , 95(8):4193-4198 (1998).
287.	Schilling, et al., "Combining Pathway Analysis with Flux Balance Analysis for the Comprehensive Study of Metabolic Systems," <u>Biotechnol Bioeng</u> , 71(4):286-306 (2000-2001).
288.	Schilling, et al., "Genome-scale metabolic model of <i>Helicobacter pylori</i> 26695," <u>J Bacteriol</u> , 184(16):4582-4593 (2002).
289.	Schilling, et al., "Metabolic Pathway Analysis: Basic Concepts and Scientific Applications in the Post-genomic Era," <u>Biotechnol Prog</u> , 15(3):296-303 (1999).
290.	Schilling, et al., "Theory for the Systematic Definition of Metabolic Pathways and Their Use in Interpreting Metabolic Function from a Pathway-Oriented Perspective," <u>J Theor Biol</u> , 203(3):229-248 (2000).
291.	Schneider, et al., "The <i>Escherichia coli</i> gabDTPC operon: specific gamma-aminobutyrate catabolism and nonspecific induction," <u>J Bacteriol</u> , 184(24):6976-6986 (2002).
292.	Schuster, et al., "A general definition of metabolic pathways useful for systematic organization and analysis of complex metabolic networks," <u>Nature Biotechnol</u> , 18(3):326-332 (2000).
293.	Schuster, et al., "Detection of elementary flux modes in biochemical networks: a promising tool for pathway analysis and metabolic engineering," <u>Trends Biotechnol</u> , 17(2):53-60 (1999).
294.	Schuster, et al., "Exploring the pathway structure of metabolism: decomposition into subnetworks and application to <i>Mycoplasma pneumoniae</i> ," <u>Bioinformatics</u> , 18(2):351-361 (2002).
295.	Schuster, S and Hilgetag, C, "On elementary flux modes in biochemical reaction systems at steady state," <u>J Biol Syst</u> , 2(2):165-182 (1994).
296.	Schwikowski, et al., "A network of protein-protein interactions in yeast," <u>Nature Biotechnol</u> , 18(12):1257-1261 (2000).
297.	
298.	

EXHIBIT A
U.S. Application No. 09/923,870

299.	Selkov, et al., "Functional Analysis of Gapped Microbial Genomes: Amino Acid Metabolism of <i>Thiobacillus Ferrooxidans</i> ," <i>Proc Natl Acad Sci U.S.A.</i> , 97(7):3509-3514 (2000).
300.	Selkov, et al., "MPW: the metabolic pathways database," <i>Nucleic Acids Res</i> , 26(1):43-45 (1998)
301.	Selkov, et al., "The metabolic pathway collection from EMP: the enzymes and metabolic pathways database," <i>Nucleic Acids Res</i> , 24(1):26-28 (1996).
302.	Shen-Orr, et al., "Network motifs in the transcriptional regulation network of <i>Escherichia coli</i> ," <i>Nat Genet</i> , 31(1):64-68 (2002).
303.	
304.	
305.	Silve, et al., "The immunosuppressant SR 31747 blocks cell proliferation by inhibiting a steroid isomerase in <i>Saccharomyces cerevisiae</i> ," <i>Mol Cell Biol</i> , 16(6):2719-2727 (1996).
306.	Skouloubris, et al., "The <i>Helicobacter pylori</i> Urel protein is not involved in urease activity but is essential for bacterial survival in vivo," <i>Infect Immun</i> , 66(9):4517-4521 (1998).
307.	Smith, et al., "Functional analysis of the genes of yeast chromosome V by genetic footprinting," <i>Science</i> , 274(5295):2069-2074 (1996).
308.	
309.	
310.	Sorlie, et al., "Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications," <i>Proc Natl Acad Sci U.S.A.</i> , 98(19):10869-10874 (2001).
311.	Stark, et al., "Amino acid utilisation and deamination of glutamine and asparagine by <i>Helicobacter pylori</i> ," <i>J Med Microbiol</i> , 46(9):793-800 (1997).
312.	Stephanopoulos, "Metabolic engineering," <i>Curr Opin Biotechnol</i> , 5(2):196-200 (1994).
313.	Summers, et al., "Saccharomyces cerevisiae cho2 mutants are deficient in phospholipid methylation and cross-pathway regulation of inositol synthesis" <i>Genetics</i> , 120(4):909-922 (1988).
314.	Swartz, "A PURE approach to constructive biology," <i>Nat Biotechnol</i> , 19(8):732-733 (2001).
315.	Syvanen, "Accessing genetic variation: Genotyping single nucleotide polymorphisms," <i>Nat Rev Genet</i> , 2(12):930-942 (2001).
316.	Szambelan, et al., "Use of <i>Zymomonas mobilis</i> and <i>Saccharomyces cerevisiae</i> mixed with <i>Kluyveromyces fragilis</i> for improved ethanol production from Jerusalem artichoke tubers," <i>Biotechnol Lett</i> , 26(10):845-848 (2004).
317.	Tamayo, et al., "Interpreting patterns of gene expression with self-organizing maps: methods and application to hematopoietic differentiation," <i>Proc Natl Acad Sci U.S.A.</i> , 96(6):2907-2912 (1999).
318.	
319.	Taniguchi, M and Tanaka, T., "Clarification of interactions among microorganisms and development of co-culture system for production of useful substances," <i>Adv Biochem Eng Biotechnol</i> , 90:35-62 (2004).
320.	Tao, et al., "Engineering a homo-ethanol pathway in <i>Escherichia coli</i> : increased glycolytic flux and levels of expression of glycolytic genes during xylose fermentation," <i>J Bacteriol</i> , 183(10):2979-2988 (2001).

EXHIBIT A
U.S. Application No. 09/923,870

321.	ter Linde, et al., "Genome-wide transcriptional analysis of aerobic and anaerobic chemostat cultures of <i>Saccharomyces cerevisiae</i> ," <i>J Bacteriol</i> , 181(24):7409-7413 (1999).
322.	Thomas, "Boolean Formalization of Genetic Control Circuits," <i>J Theor Biol</i> , 42(3):563-585 (1973).
323.	Thomas, "Logical Analyses of Systems Comprising Feedback Loops," <i>J Theor Biol</i> , 73(4):631-656 (1978).
324.	Thomas, D and Surdin-Kerjan, Y, "Metabolism of sulfur amino acids in <i>Saccharomyces cerevisiae</i> ," <i>Microbiol Mol Biol Rev</i> , 61(4):503-532 (1997).
325.	Tomb, et al., "The complete genome sequence of the gastric pathogen <i>Helicobacter pylori</i> ," <i>Nature</i> , 388(6642):539-547 (1997).
326.	Trotter, et al., "A genetic screen for aminophospholipid transport mutants identifies the phosphatidylinositol 4-kinase, STT4p, as an essential component in phosphatidylserine metabolism," <i>J Biol Chem</i> , 273(21):13189-13196 (1998).
327.	Uetz, et al., "A comprehensive analysis of protein-protein interactions in <i>Saccharomyces cerevisiae</i> ," <i>Nature</i> , 403(6770):623-627 (2000).
328.	Van den Berg, MA and Steensma, HY, "ACS2, a <i>Saccharomyces cerevisiae</i> gene encoding acetyl-coenzyme A synthetase, essential for growth on glucose," <i>Eur J Biochem</i> , 231(3):704-713 (1995).
329.	van Dijken, et al., "Alcoholic fermentation by 'non-fermentative' yeasts," <i>Yeast</i> , 2(2):123-127 (1986).
330.	van Dijken, et al., "Kinetics of growth and sugar consumption in yeasts," <i>Antonie Van Leeuwenhoek</i> , 63(3-4):343-352 (1993).
331.	Vanrolleghem, et al., "Validation of a Metabolic Network for <i>Saccharomyces cerevisiae</i> Using Mixed Substrate Studies," <i>Biotechnol Prog</i> , 12(4):434-448 (1996).
332.	Varma, A and Palsson, BO, "Metabolic capabilities of <i>Escherichia coli</i> . II: Optimal Growth Patterns," <i>J Theor Biol</i> , 165:503-522 (1993).
333.	Varma, A and Palsson, BO, "Metabolic capabilities of <i>Escherichia coli</i> : I. Synthesis of Biosynthetic Precursors and Cofactors," <i>J Theor Biol</i> , 165:477-502 (1993).
334.	Varma, A and Palsson, BO, "Parametric sensitivity of stoichiometric flux balance models applied to wild-type <i>Escherichia coli</i> metabolism," <i>Biotechnol Bioeng</i> , 45(1):69-79 (1995).
335.	Varma, A and Palsson, BO, "Predictions for Oxygen Supply Control to Enhance Population Stability of Engineered Production Strains," <i>Biotechnol Bioeng</i> , 43(4):275-285 (1994).
336.	Varma, A and Palsson, BO, "Stoichiometric flux balance models quantitatively predict growth and metabolic by-product secretion in wild-type <i>Escherichia coli</i> W3110," <i>Appl Environ Microbiol</i> , 60(10):3724-3731 (1994).
337.	Varma, et al., "Biochemical Production Capabilities of <i>Escherichia coli</i> ," <i>Biotechnol Bioeng</i> , 42(1):59-73 (1993).
338.	Varma, et al., "Stoichiometric Interpretation of <i>Escherichia coli</i> Glucose Catabolism Under Various Oxygenation Rates," <i>Appl Environ Microbiol</i> , 59(8):2465-2473 (1993).
339.	Varner, J and Ramkrishna, D, "Mathematical Models of Metabolic Pathways," <i>Curr Opin Biotechnol</i> , 10(2):146-150 (1999).
340.	Velculescu, et al., "Analysing uncharted transcriptomes with SAGE," <i>Trends Genet</i> , 16(10):423-425 (2000).
341.	

EXHIBIT A
U.S. Application No. 09/923,870

342.	Verduyn, "Physiology of yeasts in relation to biomass yields," <u>Antonie Van Leeuwenhoek</u> , 60(3-4):325-353 (1991).
343	Verduyn, et al., "A theoretical evaluation of growth yields of yeasts," <u>Antonie Van Leeuwenhoek</u> , 59(1):49-63 (1991).
344.	Verduyn, et al., "Energetics of <i>Saccharomyces cerevisiae</i> in anaerobic glucose-limited chemostat cultures," <u>J Gen Microbiol</u> , 136:405-412 (1990).
345.	Vissing, et al., "Paradoxically Enhanced Glucose Production During Exercise in Humans with Blocked Glycolysis Caused by Muscle Phosphofructokinase Deficiency," <u>Neurology</u> , 47(3):766-771 (1996).
346	Wang, et al., "Computer-aided baker's yeast fermentations," <u>Biotechnol and Bioeng</u> , 19(1):69-86 (1977).
347.	Wang, et al., "Computer Control of Bakers' Yeast Production," <u>Biotechnol and Bioeng</u> , 21:975-995 (1979).
348.	
349	Wen, et al., "Large-scale temporal gene expression mapping of central nervous system development," <u>Proc Natl Acad Sci U.S.A.</u> , 95(1):334-339 (1998).
350	Wiback, SJ and Palsson, BO, "Extreme pathway analysis of human red blood cell metabolism," <u>Biophys J</u> , 83:808-818 (2002).
351.	Wieczorke, et al., "Concurrent knock-out of at least 20 transporter genes is required to block uptake of hexoses in <i>Saccharomyces cerevisiae</i> ," <u>FEBS Lett</u> , 464(3):123-128 (1999).
352.	
353.	Wingender, et al., "The TRANSFAC system on gene expression regulation," <u>Nucleic Acids Res</u> , 29(1):281-283 (2001).
354.	
355.	Wong, P., et al., "Mathematical Model of the Lac Operon: Inducer Exclusion, Catabolite Repression, and Diauxic Growth on Glucose and Lactose," <u>Biotechnol Prog</u> , 13(2):132-143 (1997).
356.	Yamada, et al., "Effects of common polymorphisms on the properties of recombinant human methylenetetrahydrofolate reductase," <u>Proc Natl Acad Sci U.S.A.</u> , 98(26):14853-14858 (2001).
357.	Yeung, et al., "Reverse engineering gene networks using singular value decomposition and robust regression," <u>Proc Natl Acad Sci U.S.A.</u> , 99(9):6163-6168 (2002).
358.	Yeung, et al., <u>Bioinformatics</u> , "Model-based clustering and data transformations for gene expression data," 17(10):977-87 (2001).
359.	Yoshida, et al., "Combined transcriptome and proteome analysis as a powerful approach to study genes under glucose repression in <i>Bacillus subtilis</i> ," <u>Nucleic Acids Res</u> , 29(3):683-692 (2001).
360.	Zanella, A and Bianchi, P, "Red cell pyruvate kinase deficiency: from genetics to clinical manifestations," <u>Bailliere's Best Pract Res Clin Haematol</u> 13(1):57-81 (2000)
361	
362.	Zhu, J and Zhang, MO, "SCPD: a promoter database of the yeast <i>Saccharomyces cerevisiae</i> ," <u>Bioinformatics</u> , 15(7-8):607-611 (1999).
363	
364	Zweytick, et al., "Biochemical characterization and subcellular localization of the sterol C-24(28) reductase, <i>erg4p</i> , from the yeast <i>saccharomyces cerevisiae</i> ," <u>FEBS Lett</u> , 470(1):83-87 (2000).
365	

EXHIBIT A
U.S. Application No. 09/923,870

366.	
367.	
368.	URL ca.expasy.org/sprot/ , protein database SWISS—PROT .
369.	
370.	URL dchip.org , dChip software.
371.	URL Dictionary.com pgs 1-2 (2004), Matrix.
372.	
373.	
374.	
375.	URL genome.ad.jp/kegg/ , Kyoto Encyclopedia of Genes and Genomes database (KEGG).
376.	URL Genome.jp Website, KEGG Bacillus subtilis, 1-7 (2005).
377.	
378.	
379.	
380.	
381.	
382.	URL ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome , The NCBI Entrez Genome database